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## **Infectious disease profiles of Syrian and Eritrean migrants presenting in Europe: A systematic review**

Isenring, Egon ; Fehr, Jan ; Gültekin, Nejla ; Schlagenhauf, Patricia

**Abstract:** BACKGROUND In the past decade, a large influx of migrants presented in Europe. Their country of origin was mainly either Syria or Eritrea. Public health institutions in host countries in Europe are challenged to screen and care for migrant populations with regard to infectious diseases. **METHODS** We performed a systematic literature review (according to PRISMA guidelines) to define the infectious disease profile of migrants originating in Syria and Eritrea. **RESULTS** The search resulted in 825 papers of possible relevance for infectious diseases in migrants from Syria, of which, after screening, we included 35 in the systematic review. A further 265 papers of possible relevance for infectious diseases in Eritrean migrants were screened, of which we included 27 in the systematic review. In migrants from Syria, leishmaniasis was the most frequently reported infectious disease. In addition, colonisation with drug resistant, Gram-negative bacteria was reported. In the Eritrean migrants the infectious disease most described in the selected papers was louse-borne relapsing fever. Other frequently reported infectious diseases were scabies and Plasmodium vivax malaria. **CONCLUSION** Our systematic analysis defines the profiles of infectious diseases for migrants from Syria and Eritrea and serves as an evidence base for public health screening and care of presenting migrants.

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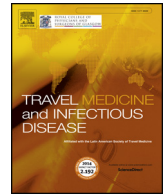


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# Infectious disease profiles of Syrian and Eritrean migrants presenting in Europe: A systematic review

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## ABSTRACT

**Background:** In the past decade, a large influx of migrants presented in Europe. Their country of origin was mainly either Syria or Eritrea. Public health institutions in host countries in Europe are challenged to screen and care for migrant populations with regard to infectious diseases.

**Methods:** We performed a systematic literature review (according to PRISMA guidelines) to define the infectious disease profile of migrants originating in Syria and Eritrea.

**Results:** The search resulted in 825 papers of possible relevance for infectious diseases in migrants from Syria, of which, after screening, we included 35 in the systematic review. A further 265 papers of possible relevance for infectious diseases in Eritrean migrants were screened, of which we included 27 in the systematic review.

In migrants from Syria, leishmaniasis was the most frequently reported infectious disease. In addition, colonisation with drug resistant, Gram-negative bacteria was reported. In the Eritrean migrants the infectious disease most described in the selected papers was louse-borne relapsing fever. Other frequently reported infectious diseases were scabies and *Plasmodium vivax* malaria.

**Conclusion:** Our systematic analysis defines the profiles of infectious diseases for migrants from Syria and Eritrea and serves as an evidence base for public health screening and care of presenting migrants.

## 1. Introduction

Since 2008, the number of refugees migrating to Europe has steadily increased. While the total number of first time asylum applicants in the European Union was around 225'000 in 2008, it rose to 1.3 million in 2015 and stayed at this level in 2016 [1]. At the end of 2016, 5.2 million refugees were hosted in European countries, with 2.9 million refugees in Turkey alone [2].

The civil war in Syria, which started in 2011 and still ongoing, with a death toll of 250'000 by 2015 [3], has resulted in a large, forcibly displaced, Syrian population, with a count of 12 million displaced persons at the end of 2016; this includes 5.5 million refugees, 6.3 million internally displaced persons (IDPs) and nearly 185,000 asylum-seekers [2].

Most Syrian migrants leave their country of origin via Turkey. While a significant number of the refugees stay in this country, others continue overland to Western Europe via Greece and the « Balkan route » [4] (Fig. 1).

87% of the Syrian refugees were accommodated in neighbouring countries and Turkey hosted the largest population of Syrian refugees (over 2.8 million). In Turkey, Syrian refugees are granted temporary protection on a group basis under the Temporary Protection regime, whereas other nationalities undergo an individual refugee status determination procedure.

Other countries in the region with significant numbers of Syrian refugees include Lebanon and Jordan. In Europe, the number of Syrian refugees is highest in Germany and Sweden. In 2016, more than 25% of the asylum seekers in the European Union were of Syrian origin [5].

A second major wave of refugees in Europe originates from Eritrea located on the Horn of Africa. Eritrea remained the ninth-largest country of origin of refugees at the end of 2016 with more than 450'000 refugees [2]. In Switzerland, Eritrean migrants constitute an important group of migrants. In 2015, 25% of all applications of asylum in Europe from Eritreans were in Switzerland [6]. This is why we chose Eritreans

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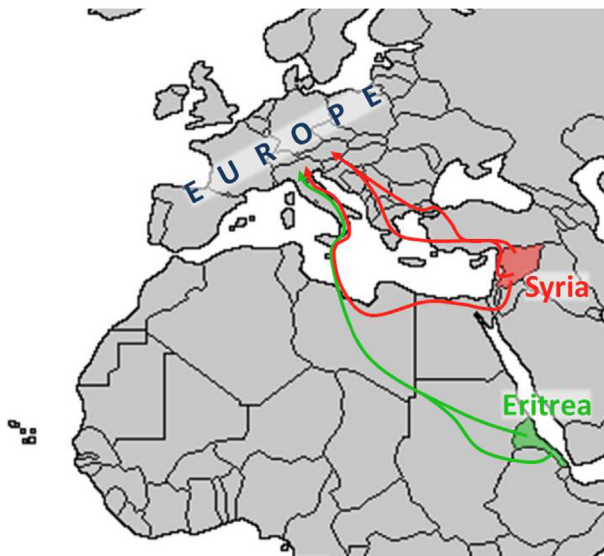


Fig. 1. Major migrant routes for Syrian and Eritrean from their country of origin to their country of destination.

Source: basic map: [www.outline-world-map.com](http://www.outline-world-map.com); Egon Isenring.

as a contrasting group to Syrians as they are likely to have a different origin, migration route and profile of infectious disease.

Since the Eritrean-Ethiopian War (1998–2000) all Eritreans are forced to serve in the „National service“ (army or civil service) for an indefinite period and without hope of leaving [6]. This forced conscription presents the major reason for Eritreans to migrate.

Eritrean migrants are usually between 15 and 30 years old. The most frequent migration route chosen by migrants from Eritrea is

through Ethiopia and/or Sudan before embarking from Libya to Europe on the “Central Mediterranean” route [7,8] (Fig. 1).

Most Eritrean refugees were hosted by Ethiopia and Sudan, but many also sought asylum further away in more northerly countries. In Europe, Sweden, Germany, Norway, the Netherlands and Switzerland represent the most important destinations for this group [6].

Due to these developments it has recently become even more important to analyze the potential infectious disease health risks, both for the migrants and for the host countries that might accompany this significant mobilization of people. Therefore the main goal of this paper is to collate data on the infectious disease profiles of Syrian and Eritrean refugees to form an evidence basis for screening programs and care strategies to address healthcare issues in migrant populations.

A secondary goal is to evaluate the extent of infectious disease risk, if any, posed to destination countries as this will have an impact on socio-political approaches to health needs in the mobile and host communities.

## 2. Methods

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and meta-Analysis (PRISMA) statement [9]. A systematic review of the literature regarding infectious diseases of migrants from Syria and Eritrea was performed using the databases PubMed, Embase, Scopus and CINAHL. The period of the study for data collection was January 2014–March 2017.

The literature search strategy included the words *infect\**, together with *migra\** or *refugee\** and *Syria\** or *Eritrea\** or a combination of the afore-mentioned terms. The asterisk was used for abridged terminology. The main author (EI) scanned the titles of all identified papers.

All citations obtained from the literature searches were scanned by one author (EI) who removed duplicates. Two authors (EI and PS) then

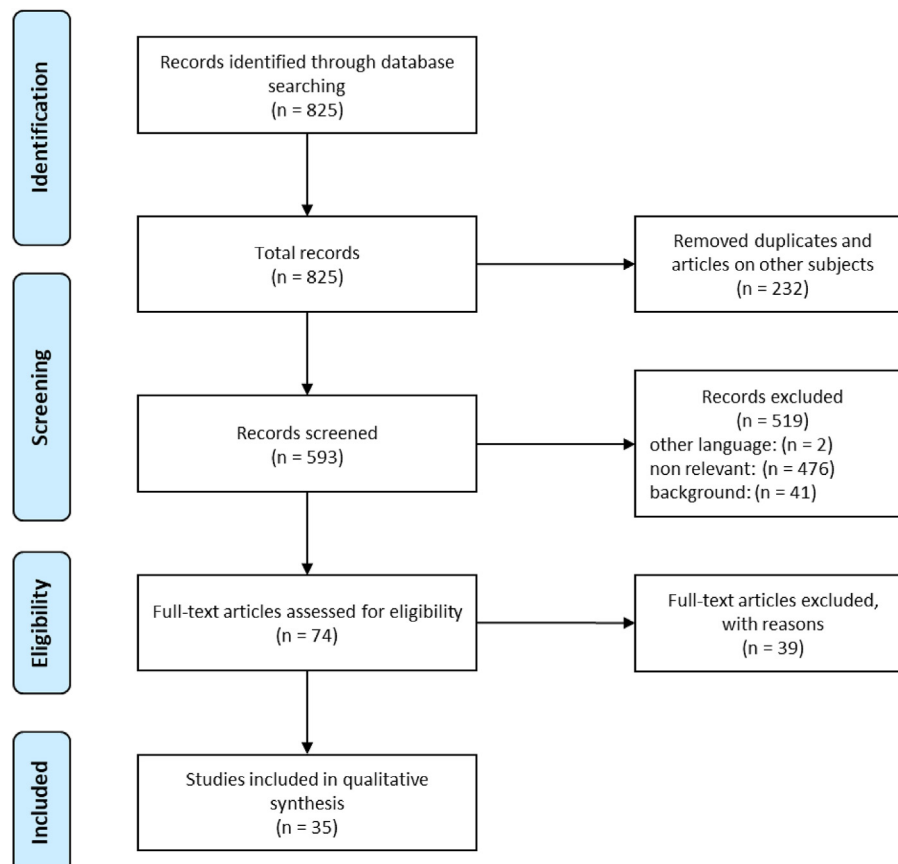


Fig. 2. Prisma flow chart for the selection of papers on infectious disease in Syrian migrants.

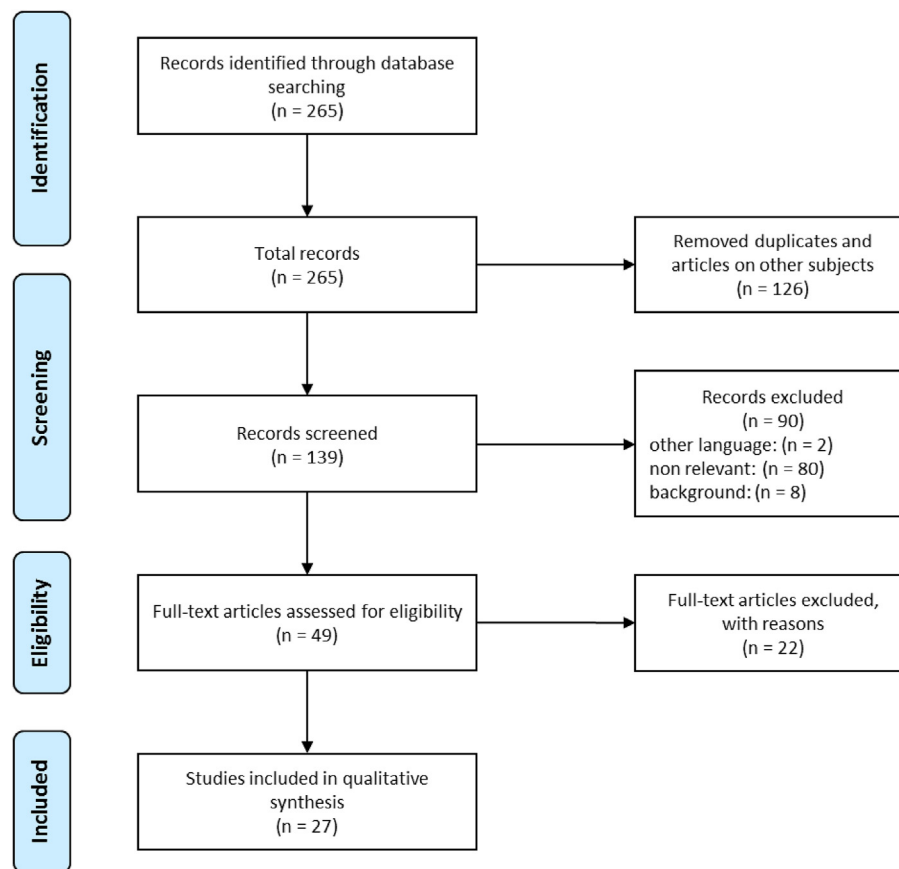


Fig. 3. Prisma flow chart for the selection of papers on infectious disease in Eritrean migrants.

scrutinised the citations in detail and made an independent selection among the full-text articles assessed for eligibility, discussed their choices and consequently agreed upon a final selection. Full-text analysis was performed for all the included articles. Finally, 35 papers of infection diseases of migrants and refugees from Syria and 27 papers concerning infections diseases of migrants and refugees from Eritrea were included in this systematic review (Prisma flow charts for both searches are shown in Figs. 2 and 3). Full details of our search strategy are provided in Appendix 1.

In papers where migrant groups were evaluated without a clear breakdown of infection according to the origin of the migrants, we contacted the corresponding authors of the respective papers to ascertain the exact details.

A dot-based, infection profile graphic was also created quantifying the numbers of papers regarding key infections divided by migrant origin in Syrian or Eritrean showing the profiles of infection according to the papers identified in the graph.

With regard to definitions used, we based these on the International Organization for Migration (IOM) definitions as follows: “Asylum-seeker” as a person who seeks safety from persecution or serious harm in a country other than his or her own and awaits a decision on the application for refugee status under relevant international and national instruments. In case of a negative decision, the person must leave the country and may be expelled, as may any non-national in an irregular or unlawful situation, unless permission to stay is provided on humanitarian or other related grounds.

“Refugee” was defined as a person who, “owing to a well-founded fear of persecution for reasons of race, religion, nationality, membership of a particular social group or political opinions, is outside the country of his nationality and is unable or, owing to such fear, is unwilling to avail himself of the protection of that country. (Art. 1(A) (2), Convention relating to the Status of Refugees, Art. 1A(2), 1951 as modified by the 1967

Protocol). In addition to the refugee definition in the 1951 Refugee Convention, Art. 1(2), 1969 Organization of African Unity (OAU) Convention defines a refugee as any person compelled to leave his or her country “owing to external aggression, occupation, foreign domination or events seriously disturbing public order in either part or the whole of his country or origin or nationality.” Similarly, the 1984 Cartagena Declaration states that refugees also include persons who flee their country “because their lives, security or freedom have been threatened by generalised violence, foreign aggression, internal conflicts, massive violations of human rights or other circumstances which have seriously disturbed public order.” [10].

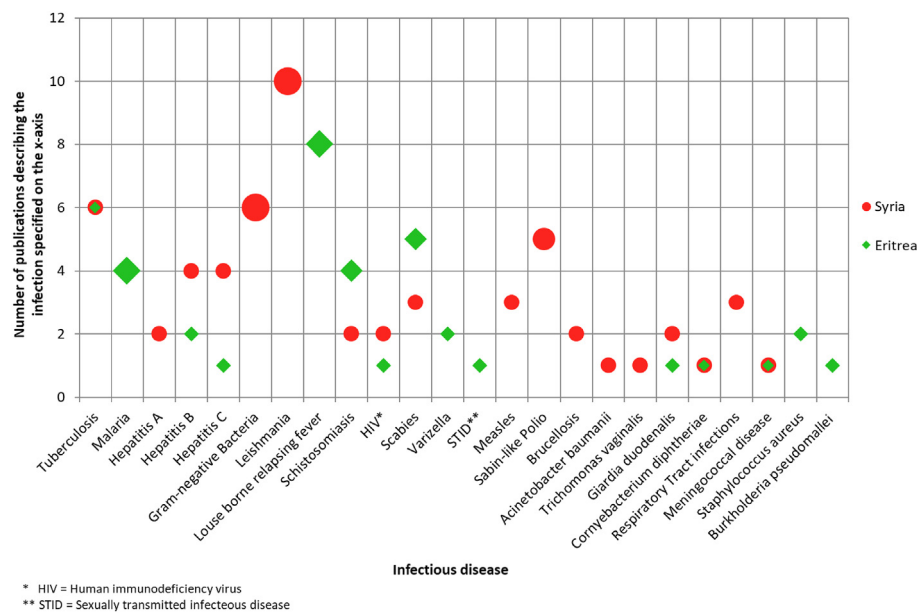
### 3. Results

For the Syrian analysis, the initial search yielded 825 records and after exclusions and duplicates, we included 35 in the final qualitative analysis (Fig. 2).

Most of the identified articles for the migrants and refugees from Syria addressed leishmaniasis ( $n = 10$ ), followed by articles containing information about tuberculosis ( $n = 6$ ), gram-negative bacteria (6) and sabin-like polio ( $n = 5$ ). Other infectious diseases which were identified in less than 5 articles (Table 1).

For the Eritrean analysis, the initial search yielded 265 records and after exclusions and duplicates, we included 27 in the final qualitative analysis (Fig. 3).

Most of the identified articles for the migrants and refugees from Eritrea addressed Louse bourne relapsing fever ( $n = 8$ ), followed by articles containing information about tuberculosis ( $n = 6$ ), scabies ( $n = 5$ ), malaria ( $n = 4$ ) and schistosoma ( $n = 4$ ) (Table 2). There were some other infectious diseases which were identified by less than 4 articles (see Fig. 4).



**Fig. 4.** Numbers of papers identified in the systematic review by infection type in Syrian and Eritrean migrants. Note: The size of the dot/diamond signifies the relevance of a particular infection for a particular migrant group.

### 3.1. Infectious disease papers addressing Syrian migrants (results)

#### 3.1.1. Leishmaniasis

The cases of leishmaniasis identified in the studies of this systematic review were equally distributed between the sexes. The majority of cases concern individuals aged less than 20 years. Most of the cases were cutaneous leishmaniasis (CL), primarily with lesions in the head and neck area and most of all on the face [11–13].

*Leishmania tropica* was the most frequently reported species. It was geographically associated with the area of Aleppo, and causes anthroponotic cutaneous leishmaniasis. *L. infantum*, localized in the coastal border of Syria, is the causative agent of the relatively rare visceral leishmaniasis. In Turkey and Lebanon, being neighbouring countries of Syria, there have also been increased incidences of rare detected types of leishmaniasis like *L. major*, which is often found in Damascus, and *L. donovani*. As for the studies reviewed, *L. tropica* and *L. major* are the most often mentioned *Leishmaniasis* species in the Syrian migrants [12,14–17].

#### 3.1.2. Colonisation with gram negative bacteria and other drug-resistant microorganisms

Several studies have used rectal, nasal and pharyngeal swabs to detect colonisation with microorganisms in Syrian refugees. Gram negative bacteria belonging to *Pseudomonas* sp., *Aeromonas* sp., *Pantoea* sp., and *Acinetobacter* sp. were the most often detected microorganisms [18]. The prevalence for multidrug-resistant Gram negative bacteria (MDR GNB) was significantly higher in the migrants than that in local populations. Moreover, the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) in migrants exceeded the rate in local non-migrant groups [18–22]. One study described two cases of NDM-1 producing *Acinetobacter baumannii* ST85 in Turkey, one of these isolates was from a Syrian refugee [23].

Another study indicated a higher prevalence of *Trichomonas vaginalis* in Syrian migrants compared to local Turkish inhabitants [24]. A further study described a Syrian migrant with *Corynebacterium diphtheriae* [25]. In addition, there was a report of an 11 years old Syrian refugee girl living in Turkey diagnosed with meningococcal meningitis type B [26]. There were two papers about brucellosis. Species identification of *Brucella melitensis* was shown in almost all cases, *B. suis* was only detected in one case [27,28]. Many scabies infections were

observed [29]. In a cohort of Syrian unaccompanied minors (UAMs) arriving in Germany the most frequent diagnosis was intestinal parasitosis. The majority were non-pathogenic parasites, 12.2% were diagnosed with *Blastocystis* spp. The pathogenic parasite most diagnosed was *Giardia duodenalis* with 7.2% [30,31]. Among fungi, unusual species such as *Alternaria alternata* and *Penicillium* were isolated [18].

#### 3.1.3. Polio

Some studies detected enteroviruses in Syrian refugees, some of these cases with the evidence of the poliovirus (PV). Intratypic differentiation of PV revealed Sabin-like Poliovirus, indicating a recent oral polio vaccination or contact to a OPV vaccinee; wild-type Poliovirus was not detected [32–35]. A seroprevalence study showed high seroprevalence against all three PV types, similar to the population living in Germany [33].

#### 3.1.4. Hepatitis

The studies show that the risk of hepatitis B and C in Syrians is very low, most of the selected studies showed no or an insignificant number of cases [18,31,36,37]. Only one study at the Syrian border to Turkey detected a significant difference between the hepatitis B incidence in Syrian refugees compared to local Turkish inhabitants and this led to the recommendation for hepatitis B screening of refugees entering Turkey [38]. The risk of hepatitis C in Syria and the Middle East is also very low except for at-risk groups such as drug users presenting high incidences [37,39]. The most common hepatitis C genotype in Syria is genotype 4 [39].

#### 3.1.5. Tuberculosis

The prevalence of active tuberculosis is very low in Syrian asylum seekers [40–43]. A study that analysed all migrants who arrived in Germany identified a higher rate (76 cases per 100,000 screened) of tuberculosis for asylum seekers compared to the general population in Germany. However, differences between the countries of origin exist: Prevalence was higher in Eritrean asylum seekers compared to Syrians. Rates in all asylum seekers are higher than in the host German population [40]. A study in Turkey showed a similar prevalence of tuberculosis in refugees from Syria compared to the Turkish population [41].



### 3.2. Infectious disease papers addressing Eritrean migrants (results)

#### 3.2.1. Louse borne relapsing fever (LBRF)

This systematic review identified several studies describing LBRF amongst Eritrean migrants [44–51]. Attendant secondary diseases were scabies and impetigo [51].

#### 3.2.2. Malaria

Both *Plasmodium vivax* and *Plasmodium falciparum* cases were reported in studies of Eritrean migrants. Most of the cases were *P. vivax*. The studies could not identify the area of acquisition of malaria or confirm whether the malaria was acquired in Eritrea or along the migration route. Three cases of *P. ovale* in Eritrean migrants were detected [7,8,43,52].

#### 3.2.3. Tuberculosis

For asylum seekers from Eritrea, active tuberculosis is more frequently reported than in Syrian migrants. Most of the cases reported in Eritreans are pulmonary TB, only a few extrapulmonary cases were detected [40,43,53–56].

#### 3.2.4. Schistosomiasis

In some studies cases of Schistosomiasis were detected in migrants from Eritrea [43,57–59]. Type specification shows in every case where it is described *Schistosoma mansoni*. One study proved the high sensitivity of point-of-care circulating cathodic antigen (POC-CCA) test on urine for *S. mansoni*. This test can improve the *S. mansoni* detection rate, but the sensitivity for detection of *S. haematobium* is not sufficiently high [57,60]. This parasitic disease has a very unspecific clinically presentation, can also present with neurologic symptoms [59].

#### 3.2.5. Scabies and other microorganisms

Several papers described scabies in migrants from Eritrea, often in combination with other infections. In one study, 14 methicillin-susceptible and one methicillin-resistant *Staphylococcus aureus* expressing the Pantone-Valentine leucocidin (PVL) are reported. In 14 of the 15 patients the clinical presentation was a skin infection. 6 cases (including 5 Eritrean migrants) presented scabies infestation and it was suggested that scabies favoured secondary infection by PVL-encoding *S. aureus* [61].

One study described 12 cases of *Corynebacterium diphtheriae*-associated wound infections in migrants from Eritrea. The microbiological analyses showed that *C. diphtheriae*-associated wound infections most often occurred together with further pathogens such as *S. aureus* and *Streptococcus pyogenes*. In 3 cases there was a co-infection with scabies [25]. Scabies also presented as co-infection of Louse-borne relapsing fever [46,51]. Scratching of the lesions increased the risk of bacterial infections [62].

One case of invasive meningococcal disease W:P1.5,2:F1-1:ST-11 in an Eritrean migrant was also described [63].

### 4. Discussion

This systematic review describes the infectious disease profile of two groups of migrants, Syrian and Eritrean, who travelled to Europe, as reported in papers identified in this systematic review of the literature.

The strongly increased emigration from Syria, a country with an above average rate of cutaneous leishmaniasis incidences amongst Arabic countries, has resulted in increased incidences of this disease in countries hosting the Syrian migrants [64]. Until 2013, leishmaniasis was rarely observed in the neighbouring countries of Syria, such as Lebanon and Turkey [15,65]. In Lebanon, the cases (found in this systematic review) were reported mainly in Lebanese districts such as the Bekaa district which is close to the Syrian border and had the highest percentage of cases (70.3%) as well the highest incidence among Syrian refugees (38 cases/100,000) [65]. In Turkey, more than

98% of the cases of CL, found in this study, are reported from the South and Southeastern Anatolian regions, thus, also in areas close to Syria [13].

Syria, itself, already a country with a significant incidence of cutaneous leishmaniasis before 2011, has seen an increase of its rate due to the civil war: on the one hand, within the population of the country itself, and also, in neighbouring countries where Syrians have migrated and often live in suboptimal conditions that favour further spread of this sandfly-borne infection. As war brings general existential insecurities and population displacement with concomitant poverty, poor housing and malnutrition and thus weakened immunity, all of which can increase the relative risk of cutaneous leishmaniasis. Concerning the current overall situation in Syria and its neighbouring countries, the increase of cutaneous leishmaniasis can be considered as the most essential deterioration of health conditions due to the Syrian civil war. The absence of an effective vaccine or any preventative drug for leishmania adds to the challenge of control and restricts containment efforts to limiting human exposure to the potential vectors and the eradication of the sandfly [65].

Counteractive measures have been applied. Systematic coordination of these activities is necessary in order to successfully identify the hot-spots and the spread of the disease, both aspects requiring a specific identification of the type of Leishmaniasis [12].

The distribution of *Leishmania* spp. overlaps with sand fly habitats and disease reservoirs. Expansive *Phlebotomus papatasi* and the *Ph. sergenti* sand fly populations exist in Syria and Iraq. Anthroponotic cutaneous leishmaniasis is caused by *L. tropica* and transmitted between humans by the *Ph. sergenti* sand fly. Zoonotic cutaneous leishmaniasis is caused by the protozoan parasite *L. major* which is transmitted through the infectious bite of the female *Ph. papatasi* and the *Ph. duboscqi* sand fly. Zoonotic visceral leishmaniasis is caused by *L. infantum* and transmitted through different species of sandflies. *Ph. orientalis* as well as *Ph. alexandri* are known as vectors of *L. donovani* which causes anthroponotic visceral leishmaniasis [15,16,64]. As far as the Arab countries are concerned, Syria is the country representing most cases of cutaneous leishmaniasis whereas Iraq reports most cases of visceral leishmaniasis [64].

In 2013 and early 2014, there was a polio outbreak in Syria with more than 30 cases. The last outbreak before was detected in 1999. In the period preceding the recent outbreak, the oral polio vaccine coverage had fallen to 52% among infants between the ages of 12–23 months nationwide. Due to mass vaccination campaigns, Syria is now approaching two years without a reported case of polio. Screening in Germany and Bulgaria only showed sabin-like poliovirus, no wild-type poliovirus was detected [32–35,66,67].

Considering the infectious disease profile of Eritrean migrants, Louse-borne relapsing fever (LBRF) caused by *Borrelia recurrentis* is strongly represented. This infection was once a major disease burden that caused major epidemics in Africa and Eurasia in the past. In the early 20th century, there were several, massive outbreaks in Eastern Europe, for example in Serbia during World War I and in Russia during the civil war. Now the infection has been restricted to East Africa for many decades with most cases reported in Ethiopia [44,48,68–70]. In 2015, around 30 cases of LBRF were diagnosed in Europe, most of these cases concerned migrants from Somalia, a few from Eritrea as well as from Ethiopia. It is difficult to determine whether the Eritrean migrants contracted the disease in their home country or on their way to Europe. Given the long duration of travel ranging from eight weeks to one year, on the one hand, and the short incubation time of 2–15 days, on the other hand, infection with *Borrelia recurrentis* was most likely acquired along the migration routes towards the end of their journeys, in Libya or Italy. The exact place of infection remains unclear. Somehow the country of origin nevertheless seems to matter as no migrants from other African regions are infected by LBRF although they increasingly share their migration routes closer they get to Europe [44,45,50,51]. This louse-borne relapsing fever is transmitted from human to human

**Table 1**  
Summary table of papers describing the Infectious disease profile of Syrian migrants.

|  |  |   |
|--|--|---|
| Meier et al. [40]<br>2016 TB   | Prospective descriptive epidemiological study<br>Case series | 11,773 newly arrived asylum seekers in Germany were investigated, about 42% (4944) came from Syria. 11 Confirmed cases of tuberculosis: 93/100'000; 1 Syrian patient had active tuberculosis. The risk of TB in Syrian migrants is low.   |
| Angeletti et al. [18]<br>2016 GNB, Hepatitis B/C, HIV  |  | 48 Syrian migrants in Italy. Rectal, nasal and pharyngeal swabs were tested: Carriage of unusual microorganisms and antimicrobial resistance was noted: mainly Gram-negative bacteria belonging to <i>Pseudomonas</i> sp., <i>Aeromonas</i> sp., <i>Pantoea</i> sp., and <i>Acinetobacter</i> sp., rarely isolated in from Italian or European subjects. Members of the genera <i>Pseudomonas</i> showed resistance to carbapenems (meropenem resistant) or extended-spectrum beta lactamase (ESBL) producers (metallo-beta-lactamase genes, such as blaVIM-1 and2). <i>Aeromonas veronii</i> resistant to meropenem was isolated from a rectal swab in one subject. <i>Staphylococcus aureus</i> , in some cases methicillin resistant was isolated. Among fungi, unusual species such as <i>Alternaria alternata</i> and <i>Penicillium</i> were isolated; Blood testing was negative for acute and chronic hepatitis B/C and for HIV.  |
| Chemaitelly et al. [39]<br>2015 Hepatitis C  | Systematic review  | Among the general Syrian population, HCV prevalence ranged between 0.3% and 0.9% (mean: 0.4%). Among Syrian populations at intermediate risk, HCV prevalence ranged between 2.0% and 5.8%. Among Syrian population at high risk: HCV prevalence was estimated at 47.4% (range: 21.0–75.0%). Genotype 4 is the most common genotype in Syria (58.2%) followed by genotype 1 (29.5%).<br>1 case: A 16 year-old female patient of Syrian origin (from Aleppo) (probably <i>L. tropica</i> ).   |
| Wollina et al. [14]<br>2015 Leishmaniasis  | Case series  | In 2013: 1033 new cases of leishmaniasis in Lebanon compared to a previous annual number in the range of 0–6 cases, 998 cases (96.6%) among Syrian refugees; January through March 2014: 217 cases of leishmaniasis, 208 involved Syrian refugees.  |
| Alawieh et al. [65]<br>2014 Leishmaniasis  | Public Health Surveillance case series                       | In 89 non-pregnant female refugees from Syria with vaginitis complaints, <i>Trichomonas vaginalis</i> infection was detected in 19 (21.3%) by direct microscopy, and in 32 (36%) by Giemsa staining of the samples. The prevalence of <i>T. vaginalis</i> (36%) in these Syrian refugees is higher than the prevalence (3–13%) of the general Turkey population.  |
| Yentür et al. [24]<br>2016 T. vaginalis  | Descriptive cross-sectional analysis case series             | 3907 asylum seekers in a study in Brussels, 20% from Syria (n = 737), mostly young men. The multiple logistic regression analysis shows that asylum seekers from Syria and children are at higher risk for infections in general; Many scabies infections observed.   |
| vanBerlaer et al. [29]<br>2016 Scabies   |  | 20 refugees with <i>Coriobacterium diphtheriae</i> -associated wound infections in Switzerland and Germany including one 38-year old from Syria, with an abscess on the right foot, the isolate was tested toxin-gene positive by PCR; no further pathogens.  |
| Meinel et al. [25]<br>2016 C. diphtheriae  | case series  | 1248 unaccompanied minor refugees arriving (UMRs) in Berlin, 40.1% (500) from Syria. Most common diagnosis of Syrian UMRs: intestinal parasitosis (22.6%) including 7.2% of <i>Giardia duodenalis</i> in addition to a majority of non-pathogenic parasites (p.e. 12.2% <i>Blastocystis</i> spp.); 9% diagnosed with a potential contagious disease; Schistosomiasis serology was positive in 1.4%; Scabies: 0.6%.  |
| Theuring et al. [30]<br>2016 G. duodenalis, Schistosomiasis, Scabies   |  | Communicable Disease cases in Syrian Refugees recorded by Ministry of Health in 2012–2015:  |
| Doganay and Demirasslan et al. [42]<br>2015 Hepatitis A, Resp. Tract infections, TB, Measles, Leishmaniasis                                    | Analysis of data of the Ministry of Health                   | <b>Diarrhea:</b> 5376 (2012) vs. 12796 (2013) vs. 28'910 (2014) vs. 54'104 (2015); <b>Hepatitis A:</b> 718 (2012) vs. 509 (2013) vs. 40 (2014) vs. 25 (2015); <b>Respiratory Tract infections:</b> 47'665 (2012) vs. 239'776 (2013) vs. 252'169 (2014) vs. 332'720 (2015); <b>Measles:</b> 31 (2012) vs. 674 (2013) vs. 114 (2014) vs. 31 (2015); <b>Tuberculosis:</b> 261 (2012) vs. 491 (2013) vs. ? (2014) vs. 558 (2015);<br><b>Leishmaniasis:</b> 109 (2012) vs. 2835 (2013) vs. 1843 (2014) vs. 718 (2015); <b>first 10 months</b> .  |
| Ismail et al. [66]<br>2016 TB, Measles, Sabin-like PV, GNB   | Review   | Secondary analysis of monitoring data from two disease early warning systems currently operational in Syria. In 2014, WHO: Tuberculosis (TB) rate: 19/100'000; 3481 cases were notified, 6.2% of new cases and 31% of treatment cases were multidrug-resistant-TB (MDR-TB). The current prevalence of TB is unknown. No cases of indigenous polio in Syria since 1995, the last laboratory-confirmed case in 1999. In 2013, the WHO detected a hot cluster of cases in Deir Ezzor, with WPV type 1 found in 2/18 cases of reported acute flaccid paralysis (AFP). Subsequently, 25 cases were reported in Deir Ezzor, 5 in Aleppo, 3 in Idlib, 2 in Al-Hasakeh, 1 in Hama. Reported oral polio vaccine (OPV3) coverage nationwide > 95% among children < 1 years of age in Syria between 2002 and 2010, but had fallen to 52% among those aged 12–23 months in the period preceding the outbreak. Transmission halted after vaccination campaigns reaching more than 2.9 Mio children < 5 y of age with repeated doses of oral polio vaccine. Vaccination with measles-containing vaccine dropped for MCV1 and MCV2 (first and second dose) from 99% coverage (WHO/UNICEF: 82%) in 2010 to 71% and 66% coverage, respectively, in 2014 (WHO/UNICEF: 54% and 49%). World Bank figures: percentage of children aged 12–23 months vaccinated for measles in Syria between 2011 and 2014 dropped from 80% to 54%; 50 new cases of suspected measles in 2014 and several thousand cases of measles were reported in Syria and Turkey in 2014. A study from Aleppo (2014) reported rates of multidrug resistant <i>Pseudomonas</i> of 54%. Reports from neighbouring countries state multidrug-resistant bacteria isolated from Syria patients up to 69%. |
| Al-Salem et al. [15]<br>2016 Leishmaniasis   | Research letter  | Cutaneous leishmaniasis prevalence coincides with the presence of refugee camps. There is a strong association between disease outbreaks and refugee settlements. Expansive <i>Phlebotomus papatasi</i> and <i>Ph. sergenti</i> sand fly populations exist in Syria and Iraq. The distribution of <i>Leishmania</i> spp. overlaps with sand fly habitats and disease reservoirs.  |
| Mockenhaupt et al. [31]<br>2016 <i>Giardia duodenalis</i> , Schistosomiasis, Hepatitis B/C, Scabies, TB, Leishmaniasis, Resp. Tract infections | Geosentinel database analysis                                | 488 unaccompanied minors (UAMs) refugees from Syria screened at the Berlin GeoSentinel site, 22% of the UAMs diagnosed with intestinal parasite, including <i>Giardia duodenalis</i> (7%), <i>Blastocystis</i> sp. (12%) and other non-pathogenic protozoa (6%). 1.4% positive serology for Schistosomiasis. 1% dental problems, 1% fungal infections, 1% anaemia, 1% abnormal urinalysis, 3% eosinophilia, < 1% scabies, < 1% upper respiratory infection. Analysis of other Syrian migrants diagnosed at GeoSentinel sites worldwide: 44 patients evaluated in eight countries; Diagnoses: cutaneous leishmaniasis (14), active (5) and latent (4) tuberculosis, chronic hepatitis (B: 3 or C: 1). Vitamin D insufficiency (4), dental problems (3), nonseptic arthritis (2), antibiotic-resistant pyelonephritis (2).<br>Distribution of multidrug-resistant Gram-negative bacteria was higher in screened refugees including Syrian refugees (N = 47) compared to resident German patients (n = 1489).  |
| Reinheimer et al. [19]<br>2016 GNB   | Cross sectional study  | 629 stool samples from Syrian refugees and asylum seekers in Germany screened for enterovirus (EV) by molecular and virological methods. 70.7% < 3years of age. 14.8% tested positive in an EV specific PCR, 12 contained Poliovirus (PV); Intratypic differentiation of PV revealed Sabin-like Poliovirus. All PV were detected in children < / = 2 years. Wild-type Poliovirus was not detected.  |
| Böttcher et al. [32]<br>2015 Sabin-like PV   | Screening study  | 68 samples of <i>Acinetobacter baumannii</i> non-susceptible to imipenem and meropenem, 2 isolates proved to carry metallo-B-lactamases and a blaNDM-1 genetic sequence. Multilocus sequences typing attributed both isolates with the sequence type (ST) 85. Case 1: 49-year old Syrian female; Case 2: 67-year old Turkey female living in Adana (close to the Syrian border).  |
| Heydari et al. [23]<br>2015 A. baumannii   | Case series  |   |

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Table 1 (continued)

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| Inci et al. [111]<br>2015 <i>Leishmaniasis</i><br>Tezer et al. [26]<br>2014 <i>Meningitis</i><br>Saroufim et al. [12]<br>2014 <i>Leishmaniasis</i>  | Retrospective study<br>Case report<br>Case series<br>Cross-sectional study<br>Case report<br>Literature search<br>Analysis of Lab data | 110 Patients diagnosed with cutaneous leishmaniasis in one Turkish hospital, 69% were Syrian refugees, living in tent camps; Highest prevalence in the 0–20 years age group (52.7%); The lesions were located on the face in 72%; 70% had a single lesion (mean lesion size was 3.7 ± 2.9 cm); The noduloulcerative lesions were the most common form of lesions (54%). Report of an 11-year-old Syrian refugee girl living in Turkey diagnosed with meningococcal meningitis type B.<br><br>1275 Syrian refugees in Lebanon, 948 were triaged for Leishmania diagnosis confirmation; 67.3% from Aleppo, 80% < 18 years of age; 77% reported the appearance of the first lesion after being in Lebanon for > 2 months, All patients had active lesions without evidence of healing or scarring; PCR yielded <i>Leishmaniasis tropica</i> in 85% of patients and <i>L. major</i> in 15%.<br><br>25/596 asylum seekers (2.3%) in Saarland, 87% from Syria. 92 anal/rectal swabs for screening of multidrug-resistant gram negative bacteria, 16 were 3MRGN <sup>+</sup> positive (17.4%), and an additional 22 were positive for 2 MGRN (24%); Patients of a tertiary care hospital in Saarland showed a local prevalence of 3.7% for 3 MGRN. 79 nasal/throat swabs for screening of methicillin-resistant <i>Staphylococcus aureus</i> (MRSA), 13 were positive (16.5%). The local patients had a prevalence for MRSA of 2.1%. All results show a burden with antibiotic resistant bacteria significantly higher in refugees than in the native high risk population. *3MRGN = gram-neg. rods with resistance against penicillin, 3 gen. cephalosporins and quinolones; 2MRGN = scheme for pediatrics without the attention to quinolones.<br><br>Between January 2015 and June 2016, 60 cases of brucellosis in Germany were reported to the Robert Koch Institute. One case was a pregnant, teenage female refugee from Syria; Blood cultures revealed <i>Brucella melitensis</i> .<br><br>Anti HAV antibody seropositivity rate in Syria: 6–10 year age group: 50%, 11–20 year age group: 81%, 21–50 year age group: 94–95%, 50 + year age group: 97–100%. |
| Grunow et al. [27]<br>2016 <i>Brucellosis</i><br>Koroglu et al. [79]<br>2015 <i>Hepatitis A</i><br>Pfalzgraf et al. [28]<br>2016 <i>Brucellosis</i>   | Case report<br>Literature search<br>Analysis of Lab data   | The national consultant lab in Germany detected 22 cases of brucellosis in 2014 and 33 cases in 2015 (m.f.3:1); Species identification of cultivated organisms yielded <i>Brucella melitensis</i> in 51 cases and <i>B. suis</i> in one case (2014). 16 refugees among the cases in 2015, most of them from Syria. Only one case in 2014 but 8 cases in 2015 in the age group < 18 years, six of the 2015 cases originating from Syria. In 2014, most of the infections were associated with an origin in Turkey, in 2015 Syria was the country with the highest case numbers (n = 12/33). The cases showed a high rate (45% and 58% in 2014 and 2015, respectively) of chronic infections.<br><br>587 sera from asylum seekers from Afghanistan, Iraq, Pakistan, Somalia and Syria examined for poliovirus (PV) neutralizing antibodies (median age: 25years): seroprevalence rates: PV1: 96.8%; PV2: 99.5%; PV3: 91.5; Independent from age and country of origin, protecting antibodies were detected in at least 93% for PV1 and PV2 and 89% for PV3 of asylum seekers examined: High seroprevalence against all three PV types, similar to the population living in Germany. Therefore, a general screening for PV is not recommended. In case of unknown vaccination status: vaccination according to existing recommendations.  |
| Neubauer et al. [33]<br>2016 <i>Sabin-like PV</i>   | Sera analysis  | At border crossing points in Turkey, a symptom-based screening was implemented for urgent health problems and children were included in the national vaccination programs compromising oral polio, measles (MMR), Tdap-Hib-IPV, hepatitis B and conjugated pneumococcus. Polio and measles coverage extended above 90%. Ministry of health: 5505 cases of cutaneous leishmaniasis, 558 cases of tuberculosis. Tuberculosis was screened in 10689 refugees: the prevalence was similar to the Turkish population (18.7/100,000). No case of malaria. A significant increase in cases of measles, particularly in southeastern region where the camps are located. Breakdown of healthcare infrastructure → outbreaks of Hepatitis A, typhoid fever and Cholera in Syria. Increasing number of cutaneous leishmaniasis cases in Turkey and Lebanon, tuberculosis in Lebanon and Jordan among refugees.   |
| Leblebicioglu et al. [41]<br>2016 <i>Leishmaniasis</i> , TB, Measles  | Review of Ministry of Health Records   | 375 Syrian refugees in north Jordan; Most frequent diagnosis: infectious diseases (30.7%), mainly upper respiratory tract infections in > 1/3 of the population and 1/2 of the children < 10 years. NSAIDs (20%), anti-infective drugs (19%) and anti-hypertensive drugs (11%) were the most dispensed medications. Anti-infective drugs accounted for 33% of total prescriptions of the age group 0–10 years and 25% of the age group 11–20y. The majority of anti-infective prescriptions were antibiotics. 1 case of hepatitis B. In Munich 219 migrants were screened yielding 53 cases of tuberculosis → 43 pulmonary; 4 of which were from Syria. 10 extrapulmonary, 1 from Syria. At the general medical office of REFUDOS in the Munich initial reception facilities, 1 case of pulmonary from Syria was identified.   |
| Gammoh et al. [36]<br>2016 <i>Hepatitis B</i> , Resp. Tract Infections<br>Alberer et al. [43]<br>2015 TB<br>Dilger et al. [38]<br>2015 <i>Hepatitis B</i><br>Salman et al. [13]<br>2014 <i>Leishmaniasis</i><br>Stoyanova et al. [34]<br>2014 <i>Sabin-like PV</i><br>Sahli et al. [21]<br>2016 GNB | cross-sectional retrospective chart review study retrospective data analysis<br>Case series<br>case series<br>Screening<br>Review      | 251 Syrian refugee patients (130 female, aged 18–75 years) were screened at the Syrian border of Turkey for HBV infection. There was a statistically significant higher prevalence of HBs antigen seropositivity (p < 0.005) in Syrian migrants.<br><br>> 98% of the cases of cutaneous leishmaniasis (CL) in Turkey were reported in the local Turkish population from South and Southeastern Anatolian regions. A significant number of Syrian migrants admitted to Nizip state hospital also tested positive for CL.<br><br>155 fecal samples of children < 5 years, from Syria and other Arab countries, residing in Bulgaria were screened for enterovirus (EV) using RT-PCR. The 3 detected polio virus isolates were Sabin-like (vaccine) PV, no wild-type PV detected.<br><br>Microbiology of war-related wound infections and factors affecting their incidence from conflict areas in Iraq, Syria, Israel and Lebanon. A study by Doctors Without Borders of 61 Syrian orthopaedic patients with suspected infections found that 74% had at least one positive wound culture, 13% of which were polymicrobial. Gram negative organisms accounted for 56% of cultures with <i>Pseudomonas aeruginosa</i> in 23%, <i>Escherichia coli</i> in 19% and <i>Acinetobacter baumannii</i> -calcoacetatus complex (ABC) in 14%. Gram-positive bacteria, including methicillin-resistant <i>Staphylococcus aureus</i> (MRSA), represented 44% of isolates. Overall, 69% of patients harboured multidrug resistant (MDR) organisms with MRSA representing 42% of staphylococcal isolates.   |
| Tenenbaum et al. [22]<br>2016 GNB   | retrospective observational study  | 325 pediatric refugees in Germany → 51.8% from Syria. 33.8% (110 refugee patients) positive multidrug-resistant organisms (MDRO) screening results → 113 isolates (83.1%) were colonized with multidrug-resistant Gram-negative (MRGN) bacteria. 87 isolates 2MRGN/ESBL (extended-spectrum B-lactamase) (63.9%), 24 isolates 3MRGN (17.7%), 2 isolates 4MRGN (1.5%); 22 isolates methicillin-resistant <i>Staphylococcus aureus</i> (MRSA) (16.2%), 1 isolate vancomycin-resistant enterococci (VRE) (0.7%).<br><br>20 asylum seeker reception center in Germany (RC), 33,874 asylum seekers, 236 asylum seekers < 3y from Syria, 4604 asylum seekers > 3y from Syria. No detection of a wild-type poliovirus.   |
| Zeitmann et al. [35]<br>2016 <i>Sabin-like PV</i><br>Kollas et al. [16]<br>2014 <i>Leishmaniasis</i>  | Electronic questionnaire<br>Screening analysis   | In Turkey, smear samples were taken from 167 cutaneous leishmaniasis (CL)-suspected cases, Bone marrow samples from 113 visceral leishmaniasis (VL)-suspected cases. Samples were analysed through real-time PCR and ITS1 DNA sequencing: Cutaneous leishmaniasis: 64.1% (107/167) positive (42.1% <i>L. tropica</i> , 36.5% <i>L. infantum</i> , 21.5% <i>L. major</i> (61% Syrian, 39% Turkish); Visceral leishmaniasis: 55.8% (63/113) positive (60% <i>L. infantum</i> , 30% <i>L. donovani</i> (63% Syrian, 37% Turkish), 10% <i>L. tropica</i> ); The incidence of <i>L. major</i> and <i>L. donovani</i> might be associated with the Syrian refugee population, since Turkish patients infected with both species were found to be living near the refugee camps. The majority of isolates identified were <i>L. infantum</i> and <i>L. tropica</i> , which have been known to cause zoonotic VL and anthroponotic CL in western and southeastern Turkey, respectively.  |
| Mumtaz et al. [37]<br>2014 HIV, Hepatitis C   | Systematic review  | Contribution of injecting drug use as a mode of HIV transmission to the total HIV/AIDS cases in Syria: 2.4% → Syria: low level HIV epidemic (limited quality and scope of evidence). Data on HCV prevalence among PWID in Syria: 21.0–60.5% (2 Damascus studies).  |



**Table 2**  
Infections in Eritrean migrants.

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| Almog et al.<br>2016 <i>B. pseudomallei</i>                                | Case report                                | <i>Burkholderia pseudomallei</i> isolated in a 45y-old Eritrean migrant worker in Israel.  |
| Meier et al. [40]<br>2016 TB   | Prospective descriptive epidemiology study | 11,773 newly arrived asylum seekers in Germany were investigated, about 1% came from Eritrea. 11 Confirmed cases of tuberculosis: 93/100'000; 5 Eritrean patients had active tuberculosis (ca 45% of detected active TB cases).  |
| Roggelin et al. [7]<br>2016 <i>Malaria</i>                                 | retrospective study                        | 37 cases of <i>Plasmodium vivax</i> malaria between 2014–August 2015 in Eritrean refugees. There was no concomitant increase in <i>P. falciparum</i> cases. Therefore, a relative increase of <i>P. vivax</i> malaria from only 2% of all cases in 2103 to 26% in 2014 and 34% in 2015. 92% of cases were male, median age was 19 years, 35% were of minor age (< 18); One patient had a mixed infection with <i>P. falciparum</i> .   |
| Jaton et al. [61]<br>2016 <i>S. aureus</i> , <i>Scabies</i>                | case series                                | 11/15 <i>Staphylococcus aureus</i> strains belonged to only two clonal complex (CC152 and CC15). The largest cluster of 8 CC152 cases of skin infections affected mainly Eritrean (4) refugees, 2/4 with scabies. 3 patients infected by CC15 strains, all Eritreans, 1 with scabies as co-pathogen infection. 5/11 CC152/CC15 cases presented scabies infestation (all Eritrean migrants).  |
| Müller et al.<br>2016  | retrospective single-center analysis       | Patients originated in Eastern Africa (27.7%) or Western Asia (22.6%). The most common countries of origin were Eritrea (13%), Somalia (13%) and Syria (11%). Ca 50% patients were treated for infections (16.8%)  |
| Osthoff et al. [44]<br>2016 <i>LBRF</i>                                    | case series                                | 4 cases of Louse-borne relapsing fever in Switzerland: 1 from Eritrea (25 year old male): Travel route from Eritrea-Sudan-Libya-Italy-CH; No additional diagnosis, no Jarisch-Herxheimer reaction; First febrile episode in Libya.   |
| Stefanelli et al. [63]<br>2016 <i>Meningitis</i>                           | case series                                | 3 cases of invasive meningococcal disease, 1 in a 20y old woman from Eritrea. DNA extraction from cerebrospinal fluid: molecular identification of <i>Neisseria meningitidis</i> serogroup W. Multilocus sequence Typing, PorA and FetA typing: W:P1.5,2:F1-1:ST-11 clonal complex (cc) strain in all samples.   |
| Hoch et al. [45]<br>2015 <i>LBRF</i>                                       | case series                                | 15 cases (males, median age: 20 years) of Louse-borne relapsing fever from the Horn of Africa, 2 from Eritrea. LBRF most likely not acquired in their countries of origin but on migration routes, possibly Libya or Italy   |
| Wilting et al. [46]<br>2015 <i>LBRF</i> , <i>Scabies</i>                   | case series                                | 2 cases (young adults) of Louse-borne relapsing fever from Eritrea. About 80% of all new arrivals from Eritrea present clinically manifest scabies.  |
| Becker et al. [57]<br>2015 <i>Schistosomiasis</i>                          | case series                                | 2 cases of <i>Schistosoma mansoni</i> in Eritrean migrants. Use of point-of-care (POC) circulating cathodic antigen (CCA) test on urine confirmed <i>S. mansoni</i> infection in both patients.  |
| Sondén et al. [8]<br>2014 <i>Malaria</i>                                   | case series                                | 105 cases of malaria from Eritrea (84 infected with <i>Plasmodium vivax</i> , 5 with <i>P. falciparum</i> , 3 with <i>P. ovale</i> ; 13 with unspecified species). The estimated <i>P. vivax</i> incidence rate 2014: 19.5/1000 Eritrean asylum seekers and 38.2/1000 Eritrean seekers < 18y. High transmission of <i>P. vivax</i> along the route of migration: Travel route through Ethiopia and/or Sudan.   |
| Padovese et al. [53]<br>2014 TB, <i>Hep B/C</i> , <i>STID</i> , <i>HIV</i> | case series                                | 500 migrants in Maltese open centers: 8.2% from Eritrea. Out of the 49.6% Tuberculin skin test (TST)-positive migrants, 86% underwent a chest x-ray, 14.9% (32) lung abnormalities, 60% of them resulted positive to IGRA.   |
| Grande et al. [52]<br>2015 <i>Malaria</i>                                  | case series                                | STI screening: low prevalence of HBsAg (6.2%), latent syphilis (2.2%), and HCV antibodies (0.6%); negative results for HIV.  |
| Uccella et al. [54]<br>2015 TB   | A retrospective single center study        | 2013–2014: Large increase in <i>P. vivax</i> malaria attributed to increased numbers of Eritrean migrants.   |
| Mor et al. [55]<br>2015 TB   | A cross-sectional study                    | 51,287 migrants presenting in Rome. 22 Tuberculosis cases were notified (0.4/1000). 59.1% of cases had origin in Africa → 13.6% Eritrea. Active TBC prevalence among foreigners resulted low.  |
| Mammina et al. [56]<br>2014 TB   | Observational study                        | 5335 undocumented migrants from the Horn of Africa, 20.4% (1087; 59% from Eritrea) underwent Chest X-ray (CXR), 5.7% (62) of the (CXRs) had radiological findings suggestive of Tuberculosis (TB); 17.7% (11) of all suspicious CXRs diagnosed as having TB (45.4% (5) of the cases with TB are from Eritrea); 90.9% pulmonary TB, 9.1% extrapulmonary TB; Sputum-smear positive results in 27.3%, and positive culture in 72.7%; 3years follow-up: 88 migrants from the Horn of Africa were diagnosed with TB in the community after being discharged from detention where they had TB screening: 62.5% (55) Eritreans, 59 (67%) were diagnosed with pulmonary TB. CXR-based screening is a valid and cost saving tool for TB screening.  |
| Kesztyüs et al. [47]<br>2016 <i>LBRF</i>                                   | case-series                                | 2010–2013: 876 Tuberculosis cases were notified in Sicily with a mean annual notification rate of 4.44 cases per 100'000 inhabitants; The proportion of TB cases in foreign-born individuals was increasing and higher than the proportion in Italian-born. The median age of foreign-born patients was significantly lower than the Italian born (30.5 vs. 51.2 years). 82% of cases were pulmonary. Molecular typing of 151 <i>Mycobacterium tuberculosis</i> complex (MTBC) isolates identified in Palermo in 2012 and 2013 detected 14 lineages and 33 sublineages showing a different distribution among the two patients sub-populations: Wide heterogeneity of MTBC isolates. Only nine MTBC isolates (6.2%) grouped in four clusters. Two multidrug resistant (MDR) MTBC isolates identified from an Italian born elderly patient and an Eritrean young patient (Beijing lineage). |

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Table 2 (continued)

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| Kreuzberg et al. [58]<br>2015 <i>Schistosomiasis</i> , <i>Giardia duodenalis</i> ,<br><i>Hepatitis B</i>  | A retrospective study       | Between September 2014 and April 2015, 160 minor refugees (15–17y old) were screened. In 21/140 assessed blood samples, eosinophilia of more than 450/μl was found, strongly associated with sub-Saharan Africa origin ( $P = 0.007$ ). 27% (10/37) of the refugees showed blood eosinophilia and 57% (8/14), respectively, came from Eritrea ( $P = 0.00004$ ). Stool microscopy (114 samples) detected <i>Schistosoma mansoni</i> ( $n = 3$ ), <i>Giardia duodenalis</i> ( $n = 2$ ) and <i>Hymenolepis nana</i> ( $n = 1$ ). Multiplex stool PCR (98 samples) tested nine more cases positive for <i>Schistosoma</i> (total $n = 12$ (7.5%)). <i>Schistosomiasis</i> was associated with eosinophilia, origin from sub-Saharan Africa, especially Eritrea. PCR also detected 10 further infections with <i>Giardia duodenalis</i> (7.5%, 12/160). No regional preferences Anti-HBc was positive in 11.3% (18/160) of cases, three of them developed chronic hepatitis B. Anti-HBc positivity was significantly higher in refugees from Sub Sahara Africa ( $P < 0.001$ ). Eosinophilia, helminth and most protozoan infections – with the exception of giardiasis – are more frequent in refugees coming from sub-Saharan Africa than from other regions. |
| Alberer et al. [43]<br>2015 <i>Scabies</i> , <i>Malaria</i> , <i>Schistosomiasis</i> , <i>TB</i>  | retrospective study         | In Munich 219 migrants were screened yielding 53 cases of tuberculosis → 43 pulmonal; 16 of which were from Eritrea. 10 extrapulmonary, 3 from Eritrea (1 multiresistant). 53 cases of malaria: 46 <i>Plasmodium vivax</i> , 43 from Eritrea; 7 <i>P. falciparum</i> , 5 from Eritrea. 15 cases of schistosomiasis, 11 from Eritrea; Many scabies cases.   |
| Goldenberger et al. [48] 2015 LBRF  | case report                 | Report of an imported case of Louse-Borne Relapsing Fever in a young adult Eritrean refugee who presented with fever shortly after arriving in Switzerland.  |
| Antinori et al. [49]<br>2016 LBRF   | systematic review           | Up to November 2015, at least 28 cases of louse-borne relapsing fever have been diagnosed among East African refugees, all patients were male, young and all cases but 2 had recently arrived in Europe. 21 from Somalia, 5 from Eritrea, 1 from Ethiopia. In most of the cases, Libya was the last country in Africa where they had resided before arriving in Europe. Onset of symptoms was reported before the arrival in Europe in 10 out of 19 patients. Body lice infestation in 5 out of 17 patients.   |
| Colomba et al. [50]<br>2016 LBRF  | Mini review and case report | 26 cases of louse-borne relapsing fever between July and October 2015 in migrants recently arrived in Europe: 8 in Italy (3 in Sicily, 5 in Piedmont), 1 in Switzerland, 2 in the Netherlands, 15 in Germany (Bavaria). 21 cases from Somalia, 5 cases from Eritrean, one case from Ethiopia. In most Eritrean cases, infestation with lice was present. All the cases had similar clinical presentation characterized by malaise, fever, headache, myalgia, five had vomiting and three abdominal pain, one patient was afebrile. The outcome was good in all but one case died of multi-organ failure after initiation of AB Therapy despite intensive care treatment. Jarisch-Herxheimer reaction in 15 (58%) of the patients.  |
| Haas et al.<br>2014 <i>Varicella</i>  | Outbreak description        | 2500 detainees from Eritrean and Sudan in southern Israel in two facilities. 109 cases of primary <i>varicella</i> had been reported over a 7-month period: infection rate: 4.4%. The outbreak described in this study stopped within one incubation period after vaccine initiation despite an overall 15.6% vaccine refusal rate   |
| Lesens et al.<br>2016 <i>Varicella</i>  | Outbreak description        | 31 migrants. 29 were Sudanese males, two were an Eritrean husband and his pregnant wife. A total of 12 persons in this group had contracted <i>varicella</i> since they had arrived in France (Attack rate: 39%). All except one had a positive <i>varicella</i> serology (96%). All the men in the group were already immune, except for the man of Eritrean origin whose wife was pregnant (her serology was positive). In contrast to these results, all except one (the pregnant Eritrean woman) were immunized against <i>measles</i> . <i>Varicella</i> outbreaks may occur in refugees from East Africa who are scantily immunized against VZV  |
| Gautschi et al. [59]<br>2015 <i>Schistosomiasis</i><br>Meinel et al. [25]<br>2016 <i>Corn. diphtheriae</i><br><i>S. aureus</i> , <i>Scabies</i> | case report                 | <i>Schistosomiasis</i> diagnosed by Serum ELISA in a 34 year-old man from Eritrea presented with gradual onset bilateral loin and leg pain; <i>Schistosoma mansoni</i> confirmed by a stool sample. 20 refugees with <i>Corynebacterium diphtheriae</i> -associated wound infections presented in Switzerland and Germany, 12 refugees from Eritrea. <i>C. diphtheriae</i> -associated wound infections most often occurred in combination with <i>Staphylococcus aureus</i> and <i>Streptococcus pyogenes</i> . 4 cases <i>methicillin-resistant S. aureus</i> (1 Eritrean refugee). 9 cases <i>methicillin-sensitive S. aureus</i> (7 in Eritrean refugees). 15 cases <i>S. pyogenes</i> (11 in Eritrean refugees). 3 cases <i>Scabies</i> (3 in Eritrean refugees).   |
| Seilmaier et al. [51]<br>2016<br>LBRF, <i>Scabies</i>   | case series                 | August 2015 – Januar 2016: 25 patients presented in the clinic in Munich with louse-borne relapsing fever, 23 from Somalia, 2 from Eritrea. 24/25: Travel route via Sudan and Lybia over the Mediterranean sea to Italy und finally to Germany. One case from Somalia via Jemen and then via Sudan and Lybia to Europe. 6/25 <i>Scabies</i> ; Case 1 from Eritrea: secondary diseases: <i>Scabies</i> und <i>Impetigo</i> , Case 2 from Eritrea: No secondary disease. Both patients from Eritrea: No detection of the bodylouse in the clothes, no signs on the skin. In both cases the Jarisch-Herxheimer-Reaktion was described.  |

via the human body louse *Pediculus humanus humanus*. This insect prefers conditions of overcrowding and poor hygienic conditions, often observed on migration routes and in camps and thus easily explaining its recovery from the clothing in some patients. Cold weather and humidity are other important factors for the prevalence of the human body lice and so during the winter months louse-transmitted diseases are more frequently reported [44,46,48,69,70]. Our review shows that mortality is estimated at between 30% and 70% for untreated cases and 2%–6% for those receiving appropriate treatment [44,45]. Concomitant disease like malaria is common [71]. As far as the therapy of LBRF infection is concerned, this is usually performed with the antibiotic ceftriaxone and/or doxycycline. It is important to be aware of the

possible Jarisch-Herxheimer reaction: this immune reaction, including the symptoms of aggravated hypotension, tachycardia, high-grade fever and deteriorated condition, is often a result of this antibiotic therapy and should be carefully monitored [46].

An increased infection rate of scabies is another result of the poor conditions the migrants from Eritrea and Syria are confronted with during their long and strenuous migration. On their way to Europe, a lot of asylum seekers stayed in several different camps and were often forced to sleep in places with poor hygiene thus significantly increasing their exposure to scabies [29] [72]. As was found in our review, 80% of the Eritrean arrivals are infected by scabies. This is why, simultaneously to the delousing because of the LBRF, arrivals are often treated with a

single dose of ivermectin as pre-emptive treatment. Those with clinically manifested scabies receive a second dose a week later [46].

As far as malaria is concerned, Eritrean migrants when arrived in Europe are mostly diagnosed with *P. vivax* malaria although *P. falciparum* is the dominant species in their country of origin. Migrants may have received schizontocidal anti-malarials (that eliminate *P. falciparum* and the blood stages of *P. vivax*) prior to, or during travel. This may be the reason why late-onset *P. vivax* occurred in Europe. Alternatively the migrants may have acquired their *P. vivax* malaria along the migration route. Geographical hotspots of *P. vivax* transmission are likely to be situated along the route of migration [7,8,73]. Three cases of *P. ovale* were described in Eritrean migrants. They may have acquired *P. ovale* in camps in Northern Africa where many migrants from West Africa are accommodated [7].

It was found in this systematic review that the risk of active tuberculosis is low when it comes to Syrian migrants. The prevalence of TB was very low in Syria, even during the civil war (19/100'000 in 2014) and significantly higher for Syrian migrants as the TB transmission is fostered within refugee communities on their common journey to Europe [40,41,43,66]. Concerning the migrants from Eritrea more cases with active tuberculosis were detected [43,54–56]. In one study, a co-incidence of TB with HIV is described. There was one single positive case of HIV in a group of 11 TB positive persons. It was confirmed that this individual with HIV/TB co-infection originated in Ethiopia not Eritrea (personal communication Mor) [55].

A special consideration should be given to multidrug resistance (MDR) tuberculosis. Military conflicts and the resulting population conflict increase the risk of MDR, also because unfinished or rather interrupted drug therapies often happen on the migrant's way to their destination country. Early detection is of great importance in order to prevent resistant tuberculosis as the experience with migrants from Eastern Europe or other countries with high risk of MDR has clearly shown in the past [74,75].

For TB, the screening strategy is highly important if countries want to guarantee an effective as well as efficient identification: as a first step, the tuberculin skin test is used for latent TB infection screening, but has many limitations including high rates of cross-reactivity with BCG vaccination and so the specificity is very low [53]. Chest x-ray (CXR) has a high sensitivity and is a valid and cost-saving approach, but the specificity is low as well [55]. The high sensitivity allows for shorter delays between screening and the start of treatment [76]. However, CXR can miss migrants with latent TB infections that may reactivate at a later stage. Furthermore, CXR is not an appropriate tool for detecting cases of extra-pulmonary TB. Finally, the strategy of symptom-based interview is useful when it comes to identify target groups with specific risks in general but has significant limitations as a screening tool.

The risk of HIV in asylum seekers from Syria is low and can be explained by their religious rules imposing restrictive behaviour regarding sexual habits. The same applies to the risk of sexual transmitted diseases in Eritrean migrants [53]. From a total of 443 Eritrean migrants tested on arrival in Malta, none were positive for HIV and none had STI symptoms. With regard to hepatitis, 32 were positive for hepatitis B and none were positive for hepatitis C (personal communication Padovese).

This systematic review allows for the following final considerations: Because of the breakdown in the Syrian health care system, the vaccination coverage has dropped [66] and outbreaks of vaccine-preventable diseases such as polio and measles have been observed in Syria itself [77]. With regard to the migrants from Syria, it is important to note that no wild type polio has been reported. The results of this systematic

review and background literature suggest that vaccination records of the migrants should be checked and if unavailable or incomplete, then vaccination should be done in accordance with age of the migrant and the vaccination schedule of the host countries and the living conditions in the refugee/migrant camp. Vaccinations to be considered should include measles-mumps-rubella, varicella, *Haemophilus influenza B* and a booster dose of tetanus-diphtheria-polio-pertussis [72,78]. Influenza can also be considered in view of the crowded living conditions and as additional protection against both influenza and norovirus infection, supplies of hand sanitizers should be recommended. The risk of tuberculosis in the Middle East region remains low but in a refugee camp the rates of transmission can be increased and interrupted or inadequate treatment may increase the risk of MDR TB. There is no consensus in host countries with regard to TB screening and treatment and this is an area for urgent action. Currently work is under way to identify migrant vaccination practices in Europe with the goal of establishing a unified approach. One study has shown a seroprevalence of only 50% in Syrian children aged less than 10 years so hepatitis A may be a risk for this age group and age selective vaccination may be appropriate [79]. Screening for chronic hepatitis B virus infection and prior immunity as well as the vaccination can also be recommended for those who are susceptible. Our analysis shows a low prevalence of hepatitis C in Syrian migrants, except for risk groups, suggesting that hepatitis C screening is not a priority. Similarly the reports for both Eritreans and Syrians suggest a low HIV prevalence [39,53].

Furthermore, this systematic review clearly shows that for Eritrean migrants presenting with fever the most likely differential diagnoses are malaria and louse-borne relapsing fever. As the malaria type mostly detected amongst Eritrean migrants is *P. vivax*, adjunct therapy with primaquine required and the logistics of have primaquine available can be daunting as primaquine is difficult to procure in many countries. LBRF, diagnosed by spirochetes identified in stained blood films and confirmed by PCR that targets the 16SrRNA gene. LBRF must be treated with antibiotics (mainly doxycycline) [44,50]. As far as this therapy is concerned, checking for Jarisch-Herxheimer-reaction is a must.

Due to the specific circumstances of their journey with crowded conditions for a prolonged period, many migrants will present with scabies which is why a presumptive treatment of all arrivals is the most effective and efficient way to deal with this infection [46].

With regard to Syrian migrants, colonisation with resistant micro-organisms is an area of concern.

As there is no vaccine or preventive therapy against leishmaniasis, this infection easily spreads amongst refugees and it is necessary to constantly check for this disease using microscopic examination of skin lesions. Apart from the standard therapy with pentavalent antimonials it is recommended to focus on vector control and to eliminate sand-fly contamination in the geographic locations of the refugee camps thus stemming the actual cause of the disease.

## 5. Conclusions

This systematic review concludes that leishmaniasis and the colonisation with antibiotic resistant gram negative bacteria present the most relevant infectious disease challenges in Syrian migrants.

With regard to the Eritrean migrants, Louse-Borne Relapsing Fever, scabies, *Plasmodium vivax* malaria and schistosomiasis were the most frequently reported infections.

These data will be of public health value in creating evidence-based screening protocols and will enable host countries to adequately prepare to the infectious disease conditions in migrant populations.

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## Appendix

Electronic database searching for Eritrea (last search on March 31, 2017). Filter for publication date from 01.01.2014 to 31.12.2016.

- a) Pubmed: "eritrea\*", "infect\*" and migra\* retrieved 16 hits, "eritrea\*", "infect\*" and refugee\* retrieved 11 hits
- b) EMBASE: "eritrea\*", "infect\*" and migra\* searched in all fields retrieved 22 hits, "eritrea\*", "infect\*" and refugee\* retrieved 20 hits
- c) Scopus: "eritrea\*", "infect\*" and migra\* in all fields retrieved 113 hits, "eritrea\*", "infect\*" and refugee\* retrieved 82 hits
- d) CINAHL: "eritrea\*", "infect\*" and migra\* retrieved 0 hits, "eritrea\*", "infect\*" and refugee\* retrieved 1 hit

Electronic database searching for Syria (last search on March 31, 2017). Filter for publication date from 01.01.2014 to 31.12.2016.

- a) Pubmed: "syria\*", "infect\*" and migra\* retrieved 12 hits, "syria\*", "infect\*" and refugee\* retrieved 35 hits,
- b) EMBASE: "syria\*", "infect\*" and migra\* searched in all fields retrieved 41 hits, "syria\*", "infect\*" and refugee\* retrieved 76 hits
- c) Scopus: "syria\*", "infect\*" and migra\* in all fields retrieved 441 hits, "syria\*", "infect\*" and refugee\* retrieved 215 hits
- d) CINAHL: "syria\*", "infect\*" and migra\* retrieved 1 hits, "syria\*", "infect\*" and refugee\* retrieved 4 hits.

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